

What is claimed is :

CLAIMS

1. A leptin polypeptide fragment that modulates an activity of LSR, comprising at least 5 4, but not more than 50 contiguous amino acids of a polypeptide sequence selected from the group consisting of SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38 and SEQ ID NO:39, wherein said at least 4 and not more than 50 contiguous amino acids include the leptin fragment central sequence.
- 10 2. A polynucleotide encoding said leptin fragment of claim 1, or the complement of a polynucleotide encoding said leptin fragment of claim 1.
- 15 3. A recombinant vector comprising said polynucleotide of claim 2.
- 20 4. A recombinant cell comprising said polynucleotide of claim 2.
5. A pharmaceutical composition comprising said leptin fragment of claim 1 and a pharmaceutically acceptable diluent.
- 25 6. A method of preventing or treating an obesity-related disease or disorder comprising providing to an individual in need of such treatment said pharmaceutical composition of claim 5.
7. The method of claim 6, wherein said obesity-related disease or disorder is selected from the group consisting of obesity, anorexia, cachexia, cardiac insufficiency, coronary insufficiency, stroke, hypertension, atheromatous disease, atherosclerosis; high blood pressure, non-insulin-dependent diabetes, hyperlipidemia, hyperuricemia, congenital lipodystrophy, and Syndrome X.
- 30 8. A method of designing mimetics of a leptin fragment that modulates an activity of LSR, comprising:
 - (a) identifying critical interactions between one or more amino acids of said leptin fragment of claim 1 and LSR;
 - (b) designing potential mimetics to comprise said critical interactions; and

(c) testing said potential mimetics abilities to modulate said activity as a means for designing said mimetics.

9. A chimeric oligonucleotide, comprising at least 9 contiguous nucleotides from a sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID

5 NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15, and SEQ ID NO:16, wherein said at least 9 contiguous nucleotides comprise at least one amino acid codon selected from the group consisting of TTA, TTG, TCA, TCG, TAU, TAC, TGT, TGC, TGG, CAA, CAG, AGA, GAA, GAG, and GGA, and

10 wherein a point mutation is present in said codon such that said codon is a stop codon.

10. A method of inhibiting the expression of at least one subunit of LSR, comprising providing to a cell said oligonucleotide of claim 9.

15 11. A method of treating or preventing an obesity-related disease or disorder comprising providing to an individual in need of such treatment said oligonucleotide of claim 9.

20 12. A chimeric oligonucleotide, comprising at least 9 contiguous nucleotides of SEQ ID NO:1, wherein said at least 9 contiguous nucleotides comprise a single nucleotide polymorphism selected from the group consisting of A1 to A32.

25 13. A method of treating or preventing an obesity-related disease or disorder comprising providing to an individual in need of such treatment said oligonucleotide of claim 12.

14. A zinc finger protein, comprising a DNA binding domain that binds specifically to 18 nucleotides of a sequence at least 50% homologous to SEQ ID NO:1, wherein said 18 nucleotides comprise two fragments of 9 contiguous nucleotides, and wherein said fragments are separated by 0, 1, 2, or 3 nucleotides.

30 15. A polynucleotide encoding said protein of claim 14.

16. A recombinant vector comprising said polynucleotide of claim 15.

35 17. A method of treating or preventing an obesity-related disease or disorder comprising providing to an individual in need of such treatment said vector of claim 16.

18. A non-human mammal comprising said polynucleotide of claim 15.
19. A method of modulating the expression of at least one subunit of LSR, comprising providing to a cell said polynucleotide of claim 15 or a fragment of an LSR polynucleotide selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15, and SEQ ID NO:16.
- 5 20. A method of treating or preventing an obesity-related disease or disorder comprising providing to an individual in need of such treatment said polynucleotide of claim 15.
- 10 21. A recombinant cell comprising said polynucleotide of claim 15.
- 15 22. A method for selecting a compound useful for the treatment or prevention of an obesity-related disease or disorder, comprising:
(a) contacting said recombinant cell of claim 21 with a candidate compound; and
(b) detecting a result selected from the group consisting of a modulation of an activity of the Lipolysis Stimulated Receptor and modulation of expression of the Lipolysis Stimulated Receptor; as a means for
- 20 (c) selecting said compound useful for the treatment or prevention of said obesity-related disease or disorder.
- 25 23. The method of claim 22, wherein said contacting further comprises a leptin polypeptide fragment that modulates an activity of LSR, comprising at least 4, but not more than 50 contiguous amino acids of a polypeptide sequence selected from the group consisting of SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38 and SEQ ID NO:39, wherein said at least 4 and not more than 50 contiguous amino acids include the leptin fragment central sequence.
- 30 24. The recombinant cell of claim 21, wherein said recombinant cell is transfected with at least one LSR polypeptide comprising a sequence at least 75% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:17, SEQ ID NO:18, and SEQ ID NO:19.
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25. A method for selecting a compound useful for the treatment or prevention of an obesity-related disease or disorder, comprising:
- (a) contacting said recombinant cell of claim 24 with a candidate compound; and
- (b) detecting a result selected from the group consisting of a modulation of an activity of the Lipolysis Stimulated Receptor and modulation of expression of the Lipolysis Stimulated Receptor; as a means for
- 5 (c) selecting said compound useful for the treatment or prevention of said obesity-related disease or disorder.
- 10 26. The method of claim 25, wherein said contacting further comprises a leptin polypeptide fragment that modulates an activity of LSR, comprising at least 4, but not more than 50 contiguous amino acids of a polypeptide sequence selected from the group consisting of SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38 and SEQ ID NO:39, wherein said at least 4 and not more than 50 contiguous amino acids include the leptin fragment central sequence.
- 15 27. A method of selecting for genes that modulate an activity of the Lipolysis Stimulated Receptor, comprising :
- 20 (a) providing a retroviral gene library to cells that express said Lipolysis Stimulated Receptor;
- (b) contacting said cells with a ligand of said Lipolysis Stimulated Receptor ;
- (c) detecting a change in said activity of the Lipolysis Stimulated Receptor as a means for selecting for said genes.
- 25 28. The method of claim 27, wherein said ligand is a leptin polypeptide fragment that modulates an activity of LSR, comprising at least 4, but not more than 50 contiguous amino acids of a polypeptide sequence selected from the group consisting of SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38 and SEQ ID NO:39, wherein said at least 4 and not more than 50 contiguous amino acids include the leptin fragment central sequence.
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